

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
3 March 2005 (03.03.2005)

PCT

(10) International Publication Number
WO 2005/019194 A1

(51) International Patent Classification⁷: **C07D 295/16**,
217/06, 213/74, 211/16, 317/58, 213/36, 239/42, 251/46,
211/58, 265/30, A61K 31/40, 31/445, 31/472, 31/496,
31/5375

Agnes [FR/FR]; 1153 Route du Saleve, F-74560 Mon-
netier-Mornex (FR).

(21) International Application Number:
PCT/GB2004/003558

(74) Agent: **WALLS, Alan, James**; Vernalis (Oxford) Limited,
Granta Park, Abington, Cambridge CB1 6GB (GB).

(22) International Filing Date: 18 August 2004 (18.08.2004)

(25) Filing Language: English

(26) Publication Language: English

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
ZW.

(30) Priority Data:
0319917.1 23 August 2003 (23.08.2003) GB
0328632.5 10 December 2003 (10.12.2003) GB

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,
FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, ML, MR, NE, SN, TD, TG).

(71) Applicants (for all designated States except US): **VER-
NALIS (OXFORD) LIMITED** [GB/GB]; Granta Park,
Abington, Cambridge CB1 6GB (GB). **LABORATOIRES
SERONO S.A.** [CH/CH]; Z.I. de l'Ouriettaz, CH-1170
Aubonne (CH).

(72) Inventors; and

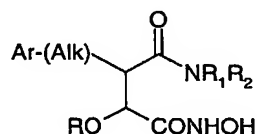
(75) Inventors/Applicants (for US only): **PAIN, Gilles**
[FR/IT]; Newron Pharmaceuticals SpA, Via Ludovico
Ariosto 21, I-20091 Bresso (IT). **DAVIES, Stephen, John**
[GB/GB]; Chroma Therapeutics Limited, 92 Milton Park,
Abindon, Oxfordshire OX14 4RY (GB). **BOMBRUN,**

Published:

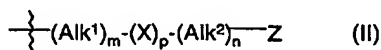
— with international search report

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: DERIVATIVES OF HYDROXAMIC ACID AS METALLOPROTEINASE INHIBITORS



(I)



(57) Abstract: Compounds of formula (I) are inhibitors of matrix metalloproteinases, and are of use in the treatment of, for example fibrotic disease, multiple sclerosis, emphysema, bronchitis and asthma: formula (I) wherein Ar represents an optionally substituted aryl, heteroaryl, C₃-C₈ cycloalkyl or heterocycloalkyl group; R represents hydrogen or C₁-C₆ alkyl, or C₃-C₆ cycloalkyl; Alk represents a divalent C₁-C₅ alkylene or C₂-C₅ alkenylene radical; and R₁ and R₂ taken together with the nitrogen atom to which they are attached form a first heterocycloalkyl ring which is optionally fused to a second C₃-C₈ cycloalkyl or heterocycloalkyl ring, the said first and second rings being optionally substituted by at least one group of formula (II): formula (II) wherein m, p and n are independently 0 or 1; Z represents, hydrogen, or an optionally substituted carbocyclic or heterocyclic ring of from 5 to 7 ring atoms which is optionally fused to another optionally substituted carbocyclic or heterocyclic ring of from 5 to 7 ring atoms; Alk¹ and Alk² independently represent optionally substituted divalent C₁-C₃ alkylene radicals; X represents -O-, -S-, -S(O)-, -S(O)₂-, -C(=O)-, -NH-, -NR₃-, -S(O)₂NH-, -S(O)₂NR₃-, -NHS(O)₂-, or -NR₃S(O)₂-, where R₃ is C₁-C₃ alkyl.